On the existence-uniqueness and computation of solution of a coupled PDE-ODE system with application to cardiac electric activity

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Abstract

In this study, we consider a system of degenerate reaction-diffusion equations, which govern the electric activity in heart with a diffusion term modelling the potential in the surrounding tissue and the nonlinear ionic model proposed by Morris & Lecar. The global existence of solution is established based on regularization argument using Fedo-Galerkin/Compactness approach. The uniqueness of the solution is shown based on Gronwell's Lemma upon some special treatment of nonlinear terms. The system of the space-time continuous model is first reduced to a semi-discrete time dependent system based on finite element Formulation and then the fully discrete system is derived using Backward Euler time stepping scheme. Numerical solution obtained using FreeFem++ are presented.

Key words: Cardiac Electric Activity, Finite Element Method, Existence-Uniqueness, ODE-PDE system.

1 Introduction

An electrocardiogram is a test that checks for the problems with the electrical activity of your heart. Bidomain model [7] is used for describing the cardiac electrical activity. It consists of two PDEs coupled to a system of ODEs, describing the electrical activity of the heart. The two PDEs describes the dynamics of intra and extracellular potentials, whereas the ODEs, also known

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as ionic model, describes the electrical behavior of the myocardium cell membrane. This model is computationally expensive because of the involvement of different space and time scales.

A simplified cardiac tissue model is the anisotropic monodomain system [7] i.e. a parabolic reaction diffusion equation describing the evolution of the transmembrane potential coupled with an ionic model. Some of the well known ionic models are FHN, Winfree, Rogers and McCulloch, Panfilov, Phase-I Luo Rudy, Morris Lecar model etc.

The first wellposedness of the Bidomain model with ionic model given by FHN ionic model [5] has been proved in [2]. In [3] and [9], existence of solution is proved for a wide class of ionic models (including Panfilov [1] and McCulloch [6]). Uniqueness however is achieved only for FHN model. In [12] existence, Uniqueness and some regularity results are proved with LR1 ionic model [4].

None of the above mentioned works consider the Morris Lecar ionic model. So, This paper describes the existence of the Bidomain model with Morris Lecar as ionic model. Main result states the existence of a global weak solution for Bidomain equation with ionic model Morris Lecar. Numerical simulation using Finite Element Method for the monodomain model with Morris Lecar ionic model is also done here. For implemantaion FreeFem++ software is used.

In the next section we descibe the mathematical model (anisotropic Bidomain and monodomain models) and ionic model also. In section 3 we state our main existence result for Bidomain equation with Morris Lecar ionic model. In section 4 we give the proof of this result. Regularization argument and Fedo-Galerkin Technique is used to proof the result. In section 5 we give some numerical results for the monodomain model with Morris Lecar ionic model.

2 Mathematical model

2.1 Bidomain model

Bidomain model is a representation of the cardiac tissue as the superposition of two anisotropic continuous media, the intra (i) and extra (e) cellular media, coexisting at every point of the tissue and connected by a distributed continuous cellular membrane. This model describes the averaged intra and extracellular electric potentials and currents by a reaction–diffusion system of degenerate parabolic type.

Let $\Omega \subset R^3$ be the bounded physical region occupied by the cardiac tissue. In

the macroscopic Bidomain representation of the cardiac tissue, the anisotropic structure of the two averaged continuous media, the intra and the extracellular medium, are characterized by the conductivity tensors D_i and D_e. Let $a_l(x), a_t(x), a_n(x)$ be a triplet of orthonormal vectors related to the structure of the myocardium at a point x, with a_l parallel to the local fiber direction and a_n normal to the muscle sheet. This triplet may depend on the position x in the myocardium. Let ${\sigma_l}^{i,e}$,${\sigma_t}^{i,e}$,${\sigma_n}^{i,e}$ be the conductivity coefficients measured along the corresponding directions. In general, these coefficients may depend on x, but in the following we assume that they are constant, i.e. homogeneous anisotropy. Then the conductivity tensors D_i and D_e, generally dependent on the position x, are given by

$$D_{i,e}(x) = {\sigma_l}^{i,e} a_l(x) {a_l}^T(x) + {\sigma_t}^{i,e} a_t(x) {a_t}^T(x) + {\sigma_n}^{i,e} a_n(x) {a_n}^T(x) \qquad (1)$$

If ${\sigma_n}^{i,e}$=${\sigma_t}^{i,e}$ we recover the axially isotropic case

$$D_{i,e}(x) = {\sigma_t}^{i,e} I + ({\sigma_l}^{i,e} - {\sigma_t}^{i,e}) a_l(x) {a_l}^T(x)$$

The biolelectric activity of cardiac cells is due to the flow I_{ion} (per unit area of the membrane surface) of various ionic currents (the most important being sodium, potassium and calcium) through the cellular membrane. Since the membrane behaves as a capacitor, the total membrane current per unit volume is given by $I_m = \chi(C_m \frac{\partial v}{\partial t} + I_{ion})$ where $v = u_i - u_e$ is the transmembrane potential, the coefficient χ is the ratio of membrane area per tissue volume, C_m is the surface capacitance of the membrane, and I_{ion} is the ionic current described later and depending on the membrane model.

Imposing the conservation of currents, we have $divJ_i = -divJ_e = I_m$ where $J_{i,e} = -D_{i,e} u_{i,e}$, are the intracellualr and the extracellular current densities. Therefore, in the Bidomain model, the intra and extracellular potentials u_i, u_e are modeled by the following reaction–diffusion system of PDEs, coupled with a system of ODEs for gating variables, descibed later. Given an applied current per unit volume $I_{app}\colon \Omega \times (0,T) \to R$, initial conditions $v_0\colon \Omega \to R$, $w_0\colon \Omega \to R^M$, find the intra and extracellular potentials $u_i, u_e\colon \Omega \to R$, the transmembrane potential $v = u_i - u_e$ and the gating variables $w_0\colon \Omega \to R^M$, such that

$$C_m \frac{\partial v}{\partial t} - div(D_i(x) \nabla u_i) + I_{ion}(v,w) = I^i_{app} \qquad in \Omega \times (0,T) \qquad (2)$$

$$C_m \frac{\partial v}{\partial t} - div(D_e(x) \nabla u_e) + I_{ion}(v,w) = I^e_{app} \qquad in \Omega \times (0,T) \qquad (3)$$

$$\frac{\partial w}{\partial t} - g(v,w) = 0 \qquad in \Omega \times (0,T) \qquad (4)$$

We assume that the cardiac tissue is insulated, therefore homogeneous Neumann boundary conditions are assigned on $\partial\Omega \times (0,T)$ as $n^T D_{i,e} \nabla u_{i,e} = 0$.

Initial conditions are assigned in Ω for $t = 0$ as follows

$$v(x,0) = u_i(x,0) - u_e(x,0) = v_0(x,0), \quad w(x,0) = w_0(x,0).$$

we then have the following compatibility condition for the system to be solvable:

$$\int_\Omega I^i_{app} = \int_\Omega I^e_{app}$$

2.2 Simplified monodomain model

Assuming equal anisotropy ratio of the two media, i.e. $D_i = \lambda D_e$ with λ constant, and setting $D = \frac{\lambda D_i}{1+\lambda}$ and $I_{app} = \frac{\lambda I^i_{app}}{1+\lambda} + \frac{I^e_{app}}{1+\lambda}$, then the Bidomain system reduces to the anisotropic Monodomain model consisting in a parabolic reaction–diffusion equation for the transmembrane potential v only

$$C_m \frac{\partial v}{\partial t} - div(D(x)\nabla v) + I_{ion}(v,w) = I_{app} \qquad in\Omega \times (0,T) \tag{5}$$

$$\frac{\partial w}{\partial t} - g(v,w) = 0 \qquad in\Omega \times (0,T) \tag{6}$$

with Neumann boundary condition for v and initial conditions for v and w.

The conductivity tensor in the axial symmetric case is given by

$$D(x) = \sigma_t I + (\sigma_l - \sigma_t) a_l(x) {a_l}^T(x) \quad \text{with} \quad \sigma_{l,t} = \frac{\lambda \sigma^i_{l,t}}{1+\lambda}.$$

This model has been extremely used in computation because it requires substantially less computational and memory resources than the Bidomain model. Nevertheless, it is not an adequate cardiac model since it is unable to reproduce some patterns and morphology of the experimentally observed extracellular potential maps and electrograms. Therefore, unequal anisotropy ratio of the intra and extracellular media cannot be neglected.

2.3 Ionic model

Morris Lecar Model [8]

Morris Lecar model is a biological neuron model developed by Dr. Catherine Morris and Dr. Harold Lecar to reproduce the variety of oscillatory behaviour in relation to $Ca^{++} and K^+$ conductance in the giant barancle muscle fiber.

It is a two dimensional system of non-linear differential equations. It is considered a simplified model compared to the four dimensional Hodgkin-Huxely model. Qualitatively, this system of equations descibes the complex relationship between membrane potential and the activation of ion channels within the membrane: the potential depends on the activity of ion channels, the activity of ion channel depends on the voltage. Ionic current and the dynamics of gating variables are given by

$$-I_{ion}(v,w) = \frac{1}{C_m}(g_{Ca}m_\infty(v)(v-v_{Ca}) + g_K w(v-v_K) + g_L(v-v_L)) \quad (7)$$

$$g(v,w) = \phi\frac{w-w_\infty(v)}{\tau_w(v)} \quad (8)$$

where

$m_\infty(v) = 0.5[1+tanh(\frac{v-v_1}{v_2})]$

$w_\infty(v) = 0.5[1+tanh(\frac{v-v_3}{v_4})]$

$\tau_w(v) = 1/cosh(\frac{v-v_3}{2v_4})$

v_L, v_{Ca}, v_K = equilibrium potential corresponding to leak , Ca^{++}, K^+ conductances, respectively.

v_1 = potential at which $m_\infty = 0.5$

v_2 = reciprocal of slope of voltage dependence of m_∞

v_3 = potential at which $w_\infty = 0.5$

v_4 = reciprocal of slope of voltage dependence of w_∞

3 Existence of the bidomain model with Morris Lecar ionic model

Assumption

(A) We Assume that the conductivities of the intracellular and the extracellular spaces D_i, $D_e \in [L_\infty(\Omega)]^{3\times 3}$ are symmetric and uniformly positive definite, i.e. there exist $\alpha_i > 0, \alpha_e > 0$ such that $\forall x \in R^3, \forall \xi \in R^3$,
$\xi^T D_i(x)\xi \geq \alpha_i |\ \xi\ |^2 \quad , \quad \xi^T D_e(x)\xi \geq \alpha_e |\ \xi\ |^2$

Notation: $V = H^1(\Omega) = \{u : u \in L^2(\Omega), Du \in L^2(\Omega)\}$

Definition 1 ***(Weak Formulation)*** *A weak solution of the Bidomain equation is a quadruplet of functions (v, u_i, u_e, w) with the regularity*

$v \in L^\infty(0,T;H^1(\Omega)) \cap H^1(0,T;L^2(\Omega))$

$u_i, u_e \in L^\infty(0,T;H^1(\Omega)), w \in W^{1,\infty}(0,T;L^\infty(\Omega))$

$$C_m \int_\Omega \partial_t v \phi_i + \int_\Omega D_i \nabla u_i \nabla \phi_i + \int_\Omega I_{ion}(v,w)\phi_i = \int_\Omega I_{app}\phi_i \tag{9}$$

$$C_m \int_\Omega \partial_t v \phi_e - \int_\Omega D_e \nabla u_e \nabla \phi_e + \int_\Omega I_{ion}(v,w)\phi_e = \int_\Omega I_{app}\phi_e \tag{10}$$

$$\partial_t w + g(v,w) = 0 \tag{11}$$

for all $(\phi_i, \phi_e) \in H^1(\Omega) \times H^1(\Omega)$ *Equations (9) and (10) holds in* $D'(0,T)$ *and equation (11) holds a.e..*

The next theorem provides the main result for the existence of solution for the Bidomain equation with Morris Lecar ionic model.

Theorem 1 *Let* $T > 0$, $I_{app} \in L^2(Q_T), D_i, D_e \in [L^\infty(\Omega)]^{3\times 3}$ *symmetric and satisfying Assumption (A),* $v_0 \in H^1(\Omega), w_0 \in L^\infty(\Omega)$ *be the given data. If* $w_0 \in L^\infty(\Omega)$ *with a positive lower bound* $r > 0$*, such that* $r < w_0 \leq 1$ *in* Ω*, then the problem (2-4) with (7), (8) and initial conditions)has a weak solution in the sense of Definition (1).*

The next section gives the proof of this theorem.

4 Proof of the theorem 3.1

The non-linear reaction diffusion equation are degenerate in time. This issue is overcome here by adding a couple of Regularization terms, making bidomain equations parabolic. Regularization and approximation of solution is merged here. Then the resulting regularized system can be analyzed through a Fedo-Galerkin/compactness procedure and a specific treatment of non-linear terms.

In section 4.1 , Regularization and Fedo-Galerkin Techniques are merged by introducing a regularized problem in finite dimension.

4.1 A regularized problem in finite dimension

Let $\{h_k\}_{k\in N^*}$ be a Hilbert basis of V. We assume that the basis functions are sufficiently smooth and that $\{h_k\}_{k\in N^*}$ is an orthonormal basis in $L^2(\Omega)$.

For all $n \in N^*$, we define the finite-dimensional space V_n generated by $\{h_k\}_{k=1}^n$ i.e.

$$V_n =< \{h_k\}_{k=1}^n >$$

Hence, we can introduce, for each $n \in N^*$, the following discrete problem associated with (9-11): **Discrete Problem** Find $(u_{i,n}, u_{e,n}) \in C^1(0,T; V_n \times V_n), w_n \in C^1(0,T; L^\infty(\Omega))$ such that, for $v_n = u_{i,n} - u_{e,n}$ and for all $(h,e) \in V_n \times V_n$ we have,

$$C_m \int_\Omega \partial_t v_n h + \frac{1}{n}\int_\Omega \partial_t u_{i,n} h + \int_\Omega D_i \nabla u_{i,n} \nabla h + \int_\Omega I_{ion}(v_n, w_n)h = \int_\Omega I_{app} h \quad (12)$$

$$C_m \int_\Omega \partial_t v_n e - \frac{1}{n}\int_\Omega \partial_t u_{e,n} e - \int_\Omega D_e \nabla u_{e,n} \nabla e + \int_\Omega I_{ion}(v_n, w_n)e = \int_\Omega I_{app} e \quad (13)$$

$$\partial_t w_n + g(v_n, w_n) = 0 a.e. in Q_T \quad (14)$$

And verifying the initial conditions

$$v_n(0) = v_{0,n}, u_{i.n}(0) = u_{i,0,n}, u_{e.n}(0) = u_{e,0,n}, w_n(0) = w_0 a.e. in \Omega \quad (15)$$

The auxiliary initial conditions for $u_{i,n}$ and $u_{e,n}$ needed, are defined by introducing two arbitrary functions $u_{i,0}$, $u_{e,0} \in V$ such that $v_0 = u_{i,0} - u_{e,0}$ in Ω. Then. for $n \in N^*$, we define $u_{i,0,n}, u_{e,0,n}, w_{0,n}$ as the orthogonal projections on $V_n \times V_n \times V_n$, of $u_{i,0}, u_{e,0}, w_0$.

By construction of these sequences, we have

$$v_{0,n}, u_{i,0,n}, u_{e,0,n}, w_{0,n} \to v_0, u_{i,0}, u_{e,0}, w_0 \ \text{ in } \ V^3 \times L^2(\Omega).$$

4.2 Local existence of the discretized solution

Lemma 4.1 *Suppose that there exists C such that*

$$\|u_{i,0,n}\|_{H^1(\Omega)} + \|u_{e,0,n}\|_{H^1(\Omega)} + \|w_{0,n}\|_{L^2(\Omega)} \leq C$$

For all $n \in N^*$ there exists a positive time $0 < t_n < T$ which only depends on C such that the Discrete problem (12)-(15) admits a unique solution over the time interval $[0, t_n]$.

Proof. Since $\{h_k\}_{k=1}^n$ is a Hilbert Basis of V_n and orthonormal basis of $L^2(\Omega)$. Since $L^\infty(\Omega) \subset L^2(\Omega)$ so $w_0, w \in L^2(\Omega)$. Now we are choosing $\theta \in V_n$ and multiplying on both side of equation (14), we get

$$\int_\Omega \partial_t w_n + \int_\Omega g(v_n, w_n) = 0 \quad (16)$$

Since $\{h_k\}_{k=1}^n$ is a Hilbert Basis of V_n and orthonormal basis of $L^2(\Omega)$. So, now we can write,

$u_{i,n} = \sum_{l=1}^n c_{i,l}(t)h_l$, $u_{e,n} = \sum_{l=1}^n c_{e,l}(t)h_l$, $w_n = \sum_{l=1}^n c_{w,l}(t)h_l$,

$u_{i,0,n} = \sum_{l=1}^n c_{i,l}^0 h_l$, $u_{e,0,n} = \sum_{l=1}^n c_{e,l}^0 h_l$, $w_{0,n} = \sum_{l=1}^n c_{w,l}^0 h_l$

Notation

$c_i = \{c_{i,l}\}_{l=1}^n$, $c_e = \{c_{e,l}\}_{l=1}^n$, $c_w = \{c_{w,l}\}_{l=1}^n$

$c_i^0 = \{c_{i,l}^0\}_{l=1}^n$, $c_e^0 = \{c_{e,l}^0\}_{l=1}^n$, $c_w^0 = \{c_{w,l}^0\}_{l=1}^n$

Then the system of equations (12),(13),(16) is equivalent to the following non-linear system of ODEs

$$M \begin{bmatrix} c_i' \\ c_e' \\ c_w' \end{bmatrix} = \begin{bmatrix} G_i(t, c_i, c_e, c_w) \\ G_e(t, c_i, c_e, c_w) \\ G_w(t, c_i, c_e, c_w) \end{bmatrix} \tag{17}$$

$$\begin{bmatrix} c_i(0) \\ c_e(0) \\ c_w(0) \end{bmatrix} = \begin{bmatrix} c_i^0 \\ c_e^0 \\ c_w^0 \end{bmatrix}$$

Here the matrix $M \in R^{3n \times 3n}$ is given by

$$M = \begin{bmatrix} (C_m + \frac{1}{n})M_V & \vdots & -C_m M_V & \vdots & 0 \\ \cdots & \vdots & \cdots & \cdots & \\ -C_m M_V & & (C_m + \frac{1}{n})M_V & \vdots & 0 \\ \cdots & & \cdots & \cdots & \\ 0 & \vdots & 0 & \vdots & M_V \end{bmatrix}$$

with $M_V \in R^{n \times n}$

and $M_V = (\int_\Omega h_k h_l)_{1 \le k,l \le n}$

and right-hand side of (17) is given by

$G_i(t, c_i, c_e, c_w) = -\int_\Omega D_i \nabla u_{i,n} \nabla h_k - \int_\Omega I_{ion}(v_n, w_n)h_k + \int_\Omega I_{app} h_k$

for all $1 \le k \le n$,

$G_i(t, c_i, c_e, c_w) = -\int_\Omega D_i \nabla u_{i,n} \nabla h_k - \int_\Omega I_{ion}(v_n, w_n) h_k + \int_\Omega I_{app} h_k$

for all $1 \leq k \leq n$,

$G_w(t, c_i, c_e, c_w) = -\int_\Omega g(v_n, w_n) h_k$

for all $1 \leq k \leq n$,

Lemma 4.2 *For all $n \in N^*$, the matrix M is positive definite.*

According to Lemma (4.2) the mass matrix M is positive definite and hence invertible and, on the other hand, the RHS of (17) is a C^1 function with respect to the arguments c_i, c_e, c_w. So, By using the Cauchy-Lipschitz theorem, existence of the local solution of the ODE system (17) follows.

4.3 Energy estimates

Lemma 4.3 *Let $u_{i,0}, u_{e,0} \in H^1(\Omega)$ and $w_0 \in L^\infty(\Omega)$ with $r < w_0 \leq 1$, there exists a positive constant w_{min} independent of T' such that a solution $(u_{i,n}, u_{e,n}, w_n)$ of the discrete problem defined on $[0, T']$ for $T' > 0$ satisfies*

$\|v_n\|_{L^\infty(0,t;L^2(\Omega))} + \frac{1}{\sqrt{n}}(\|u_{i,n}\|_{L^\infty(0,t;L^2(\Omega))} + \|u_{e,n}\|_{L^\infty(0,t;L^2(\Omega))}) + \|\nabla u_{i,n}\|_{L^2(Q_t)} + \|\nabla u_{e,n}\|_{L^2(Q_t)} \leq c$

$\|\partial_t v_n\|_{L^2(Q_t)} + \|v_n\|_{L^\infty(0,t;H^1(\Omega))} + \frac{1}{\sqrt{n}}(\|\partial_t u_{i,n}\|_{L^2(Q_t)} + \|\partial_t u_{e,n}\|_{L^2(Q_t)}) + \|\nabla u_{i,n}\|_{L^\infty(0,t;L^2(\Omega))} + \|\nabla u_{e,n}\|_{L^\infty(0,t;L^2(\Omega))} \leq c$

and, for all $t \in [0, T']$

$\|w_n\|_{W^{1,\infty}(0,t;L^\infty(\Omega))} \leq c$, $w_{min} \leq w_n \leq 1$ *in* Q_T.

Proof. From equation (14) it follows that

$\partial_t w_n = -g(v_n, w_n)$

$\partial_t w_n = -\phi \frac{w_n - w_\infty(v_n)}{\tau(v_n)}$ where $0 \leq w_\infty \leq 1$

$\partial_t w_n \geq -\phi \frac{w_n}{\tau(v_n)}$

$w_n \geq w_0 exp(-\frac{T\phi}{\tau(v_n)})$

again

$\partial_t w_n \leq -\phi \frac{w_n - 1}{\tau(v_n)} = \phi \frac{1 - w_n}{\tau(v_n)}$

$w_n \leq 1 - (1 - w_0)exp(-\frac{T\phi}{\tau(v_n)})$

using $r < w_0 \leq 1$, we obtain that

$w_{min} = rexp(-\frac{T\phi}{\tau(v_n)}) \leq w_n \leq 1$, a.e. in Q_T.

On the other hand,

$-\frac{\phi}{\tau_w} \leq \partial_t w_n \leq \frac{\phi}{\tau_w}$

$\|w_n\|_{W^{1,\infty}(0,t;L^\infty(\Omega))} \leq \frac{\phi}{\tau_w}$

For first energy estimate take $h = u_{i,n}$ and $e = u_{e,n}$ in equation (12) and (13) and then subtract, which yields

$\frac{1}{2}\frac{d}{dt}[C_m\|v_n\|^2_{L^2(\Omega)} + \frac{1}{n}(\|u_{i,n}\|^2_{L^2(\Omega)} + \|u_{e,n}\|^2_{L^2(\Omega)})] + \alpha_i\|\nabla u_{i,n}\|^2_{L^2(\Omega)}$

$+\alpha_e\|\nabla u_{e,n}\|^2_{L^2(\Omega)} + \int_\Omega I_{ion}(v_n, w_n)v_n \leq \int_\Omega I_{app}v_n$

here,

$-I_{ion}(v, w) = \frac{1}{C_m}(g_{Ca}m_\infty(v)(v - v_{Ca}) + g_K w(v - v_K) + g_L(v - v_L))$

$I_{ion}v = -\alpha v^2 - \beta v^2 w - \gamma v - \delta vw$

where, $\alpha = \frac{1}{C_m}(g_{Ca}m_\infty(v) + g_L)$, $\beta = \frac{1}{C_m}g_K$,

$\gamma = \frac{1}{C_m}(v_{Ca}g_{Ca}m_\infty(v) + g_L v_L)$, $\delta = -\frac{1}{C_m}g_K v_K$

So, $I_{ion}v \geq -\alpha^{'} \mid v \mid^2 -\gamma^{'}$ (because α and γ are bounded)

where $\alpha^{'}$ and $\gamma^{'}$ are positive constants.

Therefore,

$\frac{1}{2}\frac{d}{dt}[C_m\|v_n\|^2_{L^2(\Omega)} + \frac{1}{n}(\|u_{i,n}\|^2_{L^2(\Omega)} + \|u_{e,n}\|^2_{L^2(\Omega)})] + \alpha_i\|\nabla u_{i,n}\|^2_{L^2(\Omega)}$

$+\alpha_e\|\nabla u_{e,n}\|^2_{L^2(\Omega)} \leq (\alpha^{'} + \frac{1}{2})\|v_n\|^2_{L^2(\Omega)} + \frac{1}{2})\|I_{app}\|^2_{L^2(\Omega)} + \gamma^{'} \mid \Omega \mid$

Therefore, integrating over $(0, t)$ with $t \in [0, T']$, and after that applying Gronwall Lemma and using the fact that,

$\frac{1}{n}(\|u_{i,0,n}\|_{L^2(\Omega)} + \|u_{e,0,n}\|_{L^2(\Omega)}) + \|v_{0,n}\|^2_{L^2(\Omega)}$ is uniformly bounded with respect to n, we will get first estimate.

For the estimate of the time derivatives, we take $h = \partial_t u_{i,n}$ and $e = \partial_t u_{e,n}$ in equation (12) and (13) and subtract then integrating over $(0, t)$ with $t \in [0, T']$,

we obtain

$\frac{1}{4}C_m\|\partial_t v_n\|^2_{L^2(Q_t)}+\frac{1}{n}(\|\partial_t u_{i,n}\|^2_{L^2(Q_t)}+\|\partial_t u_{e,n}\|^2_{L^2(Q_t)})+\frac{\alpha_i}{2}\|\nabla u_{i,n}\|_{L^2(\Omega)}+\|\nabla u_{e,n}\|_{L^2(\Omega)}$

$\leq\ c(\|\nabla u_{i,0,n}\|_{L^2()\Omega)}\ +\ \|\nabla u_{e,0,n}\|_{L^2()\Omega)}\ +\ \frac{1}{2}\|I_{app}\|_{L^2(Q_t)}\ +\ \gamma^{'}T\ +\ \alpha^{'}\|v_n\|^2_{L^2(Q_t)}\ +$
$\int_0^t\int_\Omega(\beta v_n+\delta)w_n\partial_t v_n$

The last term is solved as $\int_0^t\int_\Omega(\beta v_n+\delta)w_n\partial_t v_n \leq \int_0^t\int_\Omega(\beta v_n+\delta)\partial_t v_n \leq \|(\beta v_n+\delta)\|_{L^2(Q_t)}\|\partial_t v_n\|_{L^2(Q_t)}$.

So, by inserting this inequality in the last expression and using the previous estimate we obtain the second estimate.

4.4 Global existence of solution

Energy estimates allows us to extend the existence time of our discrete solution $u_{i,n}, u_{e,n}, w_n$. According to Lemma (4.3),the solution satisfies, for all $t \in [0, T']$, where T' is the existence time

$\|u_{i,n}(t)\|_{H^1(\Omega)}\ +\ \|u_{e,n}(t)\|_{H^1(\Omega)}\ +\|w_n(t)\|_{L^2(\Omega)} \leq c$

After applying Lemma (4.1) iteratively, we obtain the existence of solution upto an arbitrary time T.

We now want to pass to the limit when n goes to infinity. Let us multiply equation (12) (13) by a function $\eta \in D(0,T)$ and integrate between 0&T. For all $k \leq n$, we have

$C_m\int_0^T\int_\Omega\eta\partial_t v_n h_k+\frac{1}{n}\int_0^T\int_\Omega\eta\partial_t u_{i,n}h_k+\int_0^T\int_\Omega\eta D_i\nabla u_{i,n}\nabla h_k$
$+\int_0^T\int_\Omega\eta I_{ion}(v_n,w_n)h_k=\int_0^T\int_\Omega\eta I_{app}h$

$C_m\int_0^T\int_\Omega\eta\partial_t v_n h_k-\frac{1}{n}\int_0^T\int_\Omega\eta\partial_t u_{e,n}h_k-\int_0^T\int_\Omega\eta D_e\nabla u_{e,n}\nabla h_k$

$+\int_0^T\int_\Omega\eta I_{ion}(v_n,w_n)h_k=\int_0^T\int_\Omega\eta I_{app}h$

From Lemma (4.3) it follows that there exists $u_i, u_e \in L^\infty(0,T;H^1(\Omega)), v \in L^\infty(0,T;H^1(\Omega))\cap H^1(0,T;L^2(\Omega)), w \in L^\infty(Q_T)$ such that

$u_{i,e,n} \to u_{i,e}$ in $L^\infty(0,T;H^1(\Omega))$ weak $*$

$v_n \to v$ in $L^\infty(0,T;H^1(\Omega))$ weak $*$

$v_n \to v$ in $H^1(0,T;L^2(\Omega))$ weak

$w_n \to$ w in $L^\infty(Q_T)$ weak $*$

According to Lemma (4.3), we also conclude that $\frac{1}{\sqrt{n}}u_{i,n}$ and $\frac{1}{\sqrt{n}}u_{e,n}$ are bounded in $L^\infty(0,T;L^2(\Omega))$. So, for all $k \in N^*$ and $\alpha \in D(0,T)$, we have

$lim_{n\to\infty}\frac{1}{n}\int_0^T\int_\Omega \eta\partial_t u_{i,n}h_k = 0$, $lim_{n\to\infty}\frac{1}{n}\int_0^T\int_\Omega \eta\partial_t u_{e,n}h_k = 0$

Since v_n is bounded in $L^2(0,T;H^1(\Omega))\cap H^1(0,T;L^2(\Omega))$, so v_n will be bounded in $H^1(Q_T)$. Hence by compact embedding of $H^1(Q_T)$ in $L^3(Q_T)$, the sequence $\{v_n\}$ strongly converges to v in $L^3(Q_T)$,

$lim_{n\to\infty}\int_0^T\int_\Omega \eta(\alpha(v_n)v_n + \gamma(v_n))h_k = \int_0^T\int_\Omega \eta(\alpha(v)v + \gamma(v))h_k$

Since sequence $\{w_n\}$ is bounded in $L^\infty(Q_T)$ and v_n strongly converges to v in $L^2(Q_T)$, we have

$lim_{n\to\infty}\int_0^T\int_\Omega \eta(\beta v_n + \delta)w_n h_k = \int_0^T\int_\Omega \eta(\beta v + \delta)w h_k$

Thus, $lim_{n\to\infty}\int_0^T\int_\Omega \eta I_{iom}(v_n,w_n)h_k = \int_0^T\int_\Omega \eta I_{ion}(v,w)h_k$

Since

$w_n \to$ w in $L^\infty(Q_T)$ weak $*$

4.5 Uniqueness of the weak solution

Lemma 4.4 *Assume that the first partial derivatives of $I_{ion}(v,w)$ and $g(v,w)$ are bounded and that $(v_1,u_{i,1},u_{e,1},w_1),(v_2,u_{i,2},u_{e,2},w_2)$ are two weak solutions of our problem corresponding, respectively , to the initial data $(v_{1,0},w_{1,0})$ and $(v_{2,0},w_{2,0})$ and right-hand sides $I_{app,1}$ and $I_{app,1}$. For all $t \in (0,T)$, there holds*

$\|v_1(t) - v_2(t)\|^2_{L^2(\Omega)} + \|w_1(t) - w_2(t)\|^2_{L^2(\Omega)}$

$\leq exp(K_1 t)K_2(\|v_{1,0} - v_{2,0}\|^2_{L^2(\Omega)} + \|w_{1,0} - w_{2,0}\|^2_{L^2(\Omega)} + \|I_{app,1} - I_{app,2}\|^2_{L^2(Q_t)})$

Proof: Ref [9]. **Remark:** This result also provides a stability estimate with respect to the initial condition.

5 Numerical method

We consider Monodomain model with Morris Lecar ionic model and consider $I_{app} = 0$. Our monodomain system is equivalent to finding $v \in H^1(\Omega)$ and

$w \in L^\infty(\Omega)$ such that

$$C_m \int_\Omega \frac{\partial v}{\partial t}\zeta - \int_\Omega D(x)\nabla v \nabla \zeta + \int_\Omega I_{ion}(v,w)\zeta = 0 \tag{18}$$

$$\int_\Omega \frac{\partial w}{\partial t}\varsigma - \int_\Omega g(v,w)\varsigma = 0 \tag{19}$$

for all $\zeta \in H^1(\Omega), \varsigma \in L^2(\Omega)$. The system is discretized in space using finite element method and in time using Backward Euler method.

5.1 Finite element discretization in space

We consider the square domain $\Omega = [a,b]^2$. The domainΩ is discretized by introducing a structured quasi-uniform grid of triangular $P1$ elements(which is denoted by τ_h). So, FEM approximation for the domain Ω is, $\Omega = \cup_{E\in\tau_h} E$.

The associated finite element space

$V_h = \{\zeta_h \in V : \zeta_h \text{is continuous in} \Omega : \zeta_{h|E} \in P_1(E), \forall E \in \tau_h\}$

A semi-discrete form is obtained by applying a standard Galerkin procedure and choosing a finite element basis $\{\zeta_i\} \in V_h$. Let I^h_{ion} be the finite element approximation of I_{ion}.

In the monodomain model, the finite element approximation v_h of transmembrane potential v and w_h of gating variable w are the solution of

$$M\frac{\partial v_h}{\partial t} + Av_h + MI^h_{ion}(v_h, w_h) = 0, \frac{\partial w_h}{\partial t} = g(v_h, w_h) \tag{20}$$

where

$M = (m_{rs}), m_{rs} = \sum_E \int_E \zeta_r \zeta_s dx$

$A = (a_{rs}), a_{rs} = \sum_E \int_E \nabla {\zeta_r}^T D(x) \nabla \zeta_s dx$

Numerical quadrature in 2-dimension is used in order to compute these integrals. Now this ODE system is discretized by Backward Euler and the implementation is done using FreeFem++ library functions [10].

To numerically simulate the transmembrane potential (v) in a cardiac tissue as modeled by the coupled PDE-ODE system (5-6) representing the monodomain model [7] for cardiac tissue together with the ionic model proposed by Morris and Lecar [8] the required parameter is chosen as given in [7] and [8] and these details are provided in the table 1 and table 2. In all the numerical simulations cardiac tissue has been represented by a square domain $\Omega = [-1.25, 1.25]^2$. To carry out the numerical simulations one has to choose an appropriate grid system so that numerical solution is computed to the acceptable accuracy. Such a goal has been achieved here through grid validation test. Three different grid systems consisting of (a) 121, (b) 441 and (c) 1681 degrees of freedom (dofs) (or (a) 200, (b) 800 and (c) 3200 number of linear triangular elements respectively) have considered. Transmembrane potential (v) obtained using these three grid systems are compared at different points of the domain. In all these cases only a marginal variation (less than 0.5%) in "v" is noticed as one moves from the grid system (a) to the grid system (c). As a sample in Fig. 1 the transmembrane potential corresponding to (x,y)=(0,0) with time are compared. Clearly the grid system with 1681 dofs is more than adequate for the current set of simulations. Hence all the simulations are carried out using 3200 linear triangular elements with 1681 dofs. In Fig. 2 the temporal variation of transmembrane potential corresponding to the following five different representative points, choosen from the four different quadrants, of the domain are presented. The initial transmembrane potential at these points follow the IC setup and they gradually evolve to the same steady state with $v \cong 2$, indicating that the intra and extra cellular potentials have reached a state which no more favour calcium and Potassium ion migration and thereby maintain stable ionic concentration in the absence of any depolarization phase. It is noticed that in about 300 time steps the transmembrane potential corresponding to all these points already reach the steady state and on further time marching only a marginal variation in v is noticed. So the entire domain is nearly re-polarized in about 300 time steps where each time step corresponds to 0.1 millisecond size. It is also to be noted lesser the initial transmembrane potential, than its steady state value, more rapid is the growth in v , due to larger driving force (potential difference), and hence all points irrespective of its starting value would reach a steady state in about 300 time steps. This also indicates that smaller the v than 2, stronger may be the migration of calcium and potassium ions. Now to trace the transmembrane potential in the entire domain in the form of isochrones or iso-potential plots for the entire domain corresponding to six different time instances covering the initial state to the steady state situation are presented in Fig. 3. From the legend values for v it is clear that the the min-max differences in v reach to a nearly zero state in about 400 time steps each of 0.1 millisecond.

6 Conclusions

We prove the Existence uniqueness for the solution of bidomain model with Morris Lecar ionic model using Galerkin and Compactness approach. Also Finite Element Computations based on Monodomain model depict the success and effectiveness of Morris Lecar ionic model in enabling the visualization the Cardiac Electric Activity in a cardiac tissue.

7 Acknowledgement

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Table 1
parameter Values used for the simulation

parameter	v_1	v_2	v_3	v_4	v_{Ca}	v_K
values	-1.2	18	-1	14.5	120	-70

Table 2
parameter Values used for the simulation

parameter	v_L	g_l	g_K	g_{Ca}	λ	σ_l	σ_t
values	-50	4	8	3	1	$1.2 * 10^{(-3)}$	$2.5562 * 10^{(-4)}$

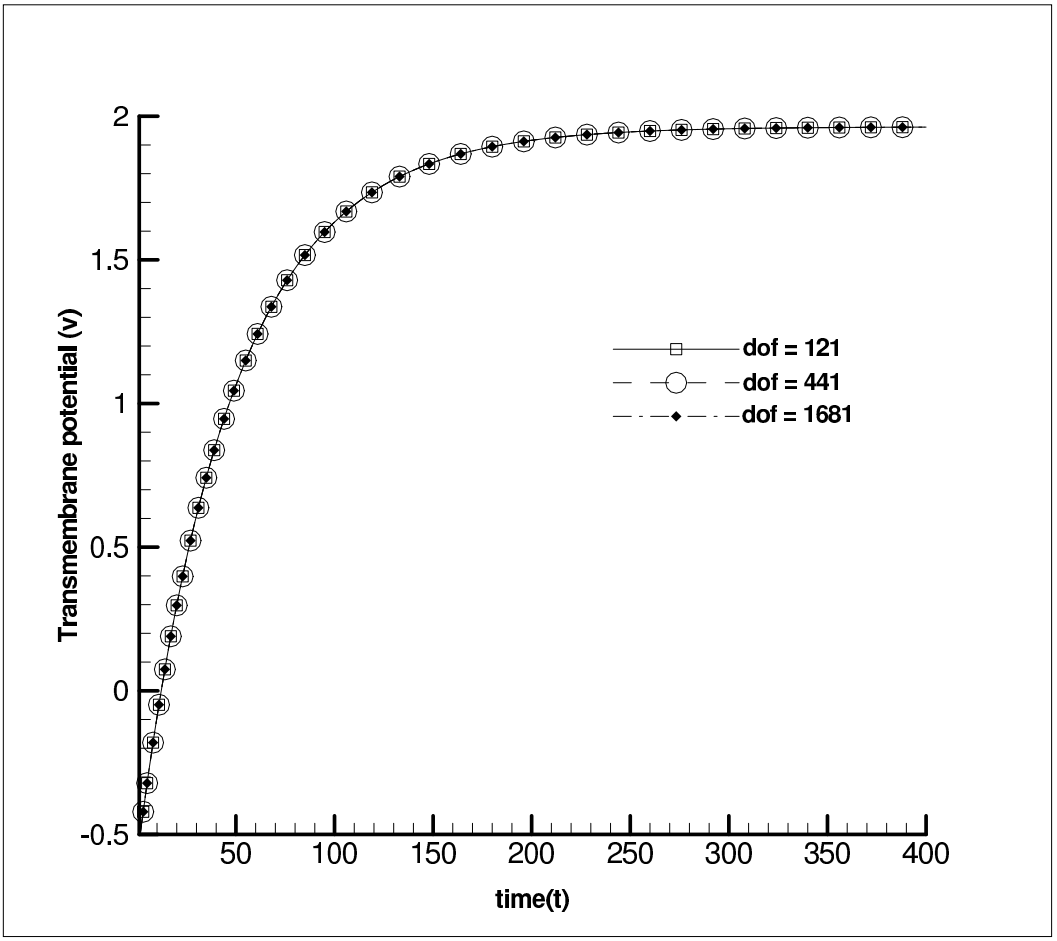

Fig. 1. plot corresponding to point (0,0) for dofs=121 , 441 , 1681.

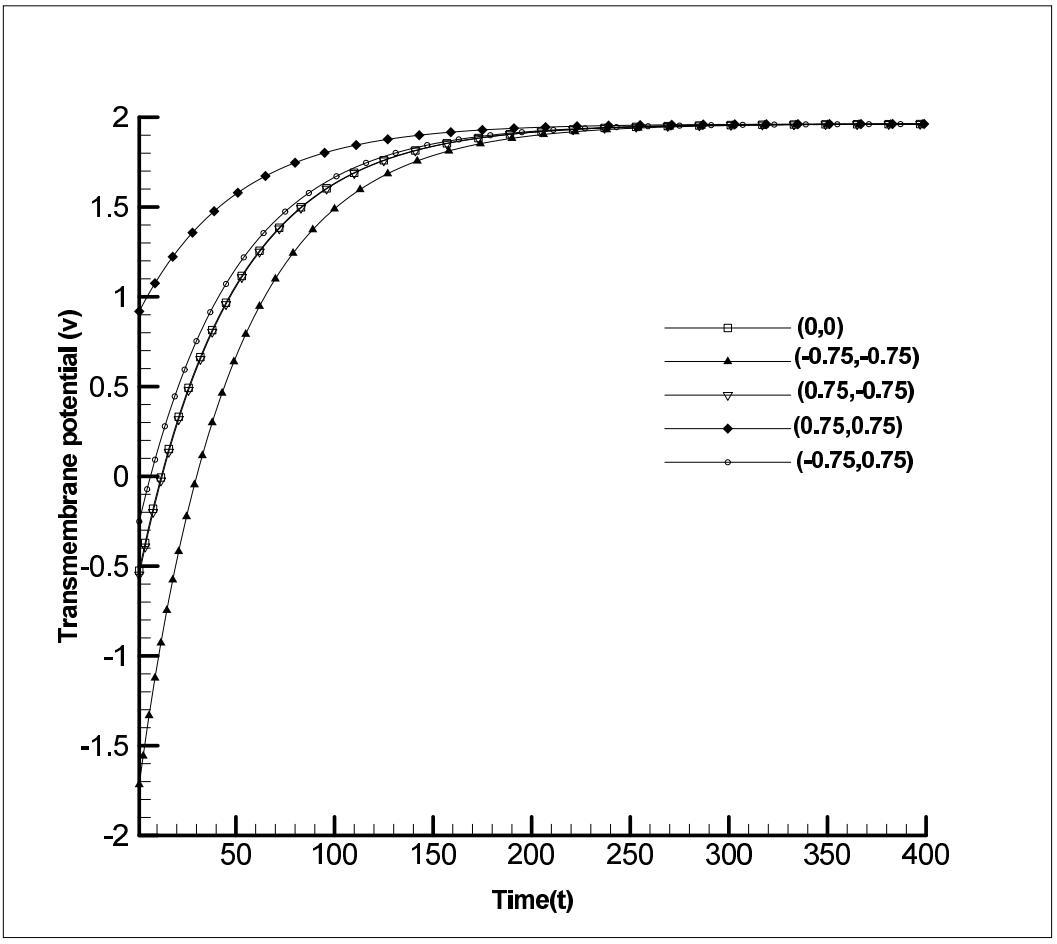

Fig. 2. plot for five different points with dof=1681.

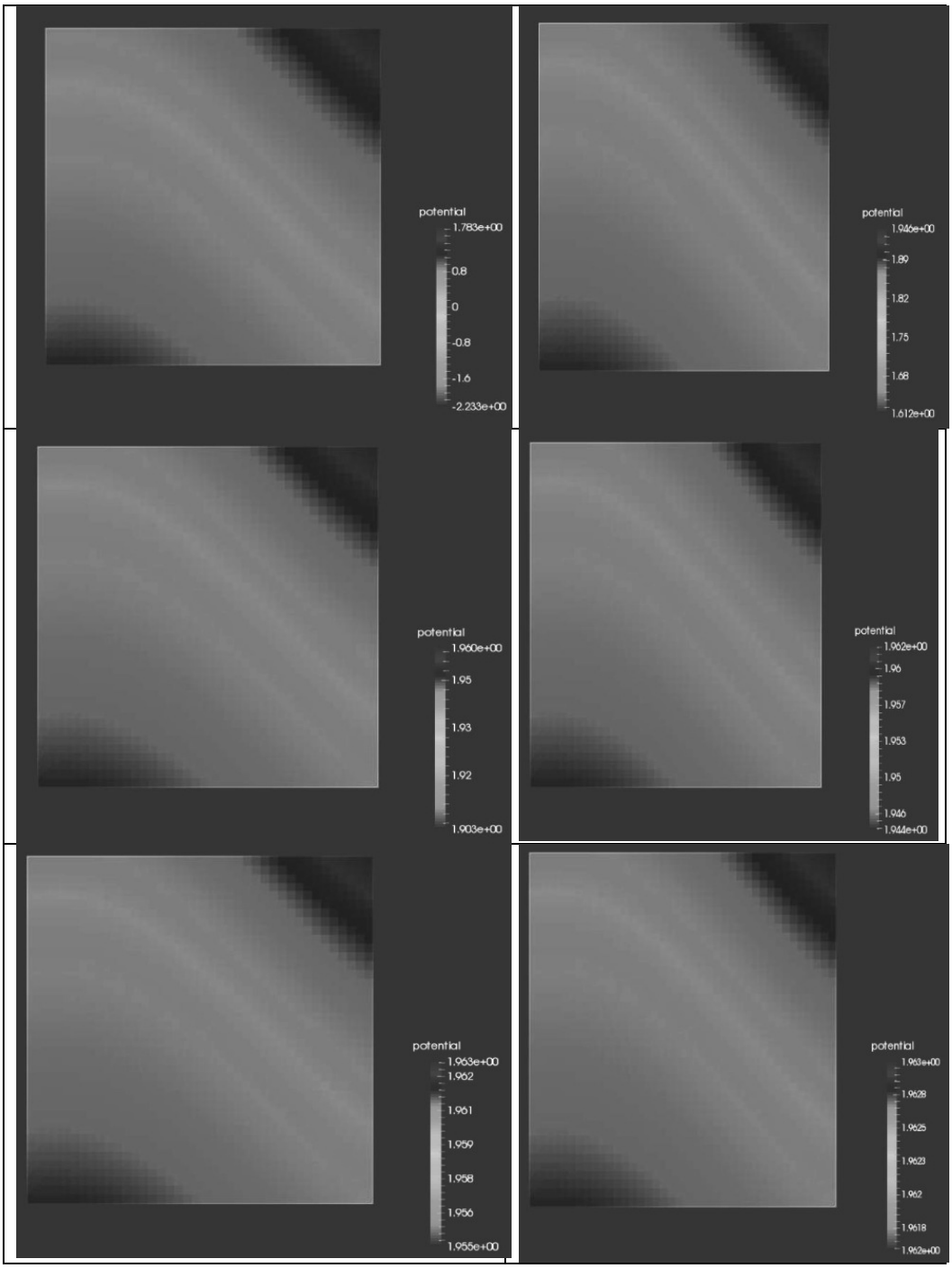

Fig. 3. the isochrones or iso-potential plots for the entire domain corresponding to six different times t=0 , 120 , 210 , 270 , 310 , 399 respectively.